

### REMARKS

Claims 1, 16, 21, 89, 95, 96, 97, and 98 are amended. Support for the term “artificially assembled” can be found throughout the specification, e.g., at page 29, line 25. Support for a library that encodes test domains that are identical to zinc finger domains from naturally occurring proteins can be found, e.g., at page 20.

The claims are currently rejected as obvious in view of Barbas et al. and Cheng et al. The Examiner indicated in the Advisory Action dated January 17, 2006 that:

**[T]he amendment of the claim to recite the limitation "non-naturally occurring protein" would obviate the art rejections of record.**

Applicants have amended the claims to refer to “artificially assembled” proteins. The term “artificially assembled” indicates that the protein is constructed by artifice. Generally an artificial protein is the product of recombinant molecular biology. For example, in the method of claim 1, an “artificially assembled” protein would be a protein created by joining a nucleic acid encoding a naturally occurring zinc finger domain with a sequence encoding the invariant DNA binding domain. Moreover, this construction juxtaposes a test zinc finger domain that is identical to a zinc finger domain from a naturally occurring protein with the unrelated amino acid sequence of the invariant DNA binding domain, resulting in an artificial protein. According to the Examiner's views quoted above, this amendment should obviate the extant art rejections.

The Examiner raised separate concerns:

**However, rejections under 35 U.S.C. 112, 1st paragraph would be made for the reasons presented on pages 5-8 of the Office action mailed 6/2/2004.**

The use of the term “artificially assembled” rather than “non-naturally occurring” obviates this concern.<sup>1</sup> There is little or no room for doubt that when one employs recombinant molecular biology to join a nucleic acid encoding a naturally occurring zinc finger domain with a sequence encoding the invariant DNA binding domain that one is artificially assembling a protein. Thus, the use of the term “artificially assembled” is not indefinite and would not run

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<sup>1</sup> Note that the USPTO's online database of patents current to March 7, 2005 revealed 480 patents that included the term “artificial” with protein or polypeptide in the claims. Search terms were “aclm/(artificial and protein) or aclm/(artificial and polypeptide).” Thus, there is no systemic indefiniteness inherent in the term “artificial” or its adverb form “artificially.”

afoul of the concerns expressed by the Examiner in the Action of June 2, 2004 regarding the alleged indefiniteness of the term "non-naturally occurring."

In addition, the Applicants do not accede to the substance of the obviousness rejection. As noted above, this rejection is traversed by adoption of the Examiner's suggestion to limit the claims. The Applicants have further amended the claims to recited that each test zinc finger domain is identical to a zinc finger domain from a naturally occurring protein. The Examiner stated in the Final Office Action dated June 20, 2005 that:

**Regarding the use of natural human zinc fingers as test zinc finger domains, it would have been obvious to do so because Barbas teaches that different zinc fingers can be used in the methods, including from proteins that are natural human proteins.**

The Applicants are unaware of which section of the Barbas patent is being referenced in the passage quoted above. Barbas emphasizes using natural zinc fingers as a starting point to create mutated zinc finger domains that are not naturally occurring. This approach would *not* result in a library in which each test zinc finger domain is identical to a zinc finger domain from a naturally occurring protein, rather it would provide a library of nucleic acids in which the test zinc finger domains deviate from those of natural zinc finger domains. Thus, the Barbas patent does not appear to teach a library of nucleic acids in which each test zinc finger domain varies and is identical to a zinc finger domain from a naturally occurring protein. The library in Cheng et al. uses completely randomized peptides that cannot be equated with natural zinc finger domains.

To establish a *prima facie* case of obviousness, the references must teach or suggest each element of the claim. The Applicants respectfully submit that neither the Barbas patent nor Cheng et al. nor even the alleged combination teach or suggest a library of nucleic acids in which each test zinc finger domain varies and is identical to a zinc finger domain from a naturally occurring protein. Therefore, the claims as presently amended are not obvious over the alleged combination of the Barbas patent and Cheng et al.

The Applicants also request thorough examination of the dependent claims. For example, with respect to claim 98, currently amended, the Applicants were unable to identify the basis of

Applicant : Jin-Soo Kim et al.  
Serial No. : 09/785,632  
Filed : February 16, 2001  
Page : 17 of 17

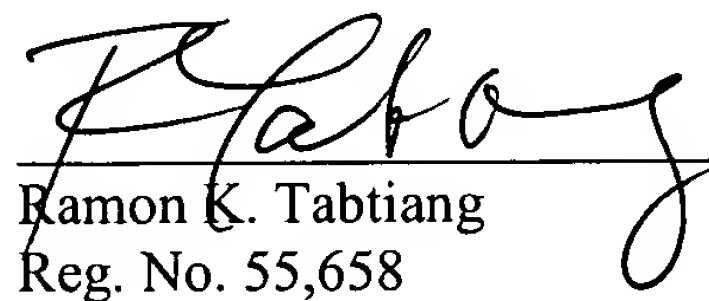
Attorney's Docket No.: 12279-002001

the Examiner's rejection. Neither the Barbas patent nor Cheng et al. appears to teach fusing cells.

Enclosed is a Request for Continued Examination, Petition for Extension of Time and the requisite fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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